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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,035	02/09/2001	Tariq Ghayer	BBC-084	8433

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EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/780,035	Applicant(s) GHAYER ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-12 and 14-61* is/are pending in the application.

4a) Of the above claim(s) *39-43 and 47-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-12,14-38,44-46 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 February 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 9/30/02 (Paper No. 11), is acknowledged.
Claims 1-3, 13 have been cancelled.
Claim 61 has been added.
Claims 4, 11, 16 and 46 have been amended.
Claims 4-12 and 14-61 are pending.

Claims 39-43 and 47-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in Paper No. 9.

Claims 4-12, 14-38, 44-46 and 61 *are under consideration in the instant application.*

2. This Office Action will be in response to applicant's arguments, filed 9/30/02 (Paper No. 11). The rejections of record can be found in the previous Office Action (Paper No. 10).

It is noted that New Grounds of Rejection are set forth herein.

3. Applicant's cancellation of claims 1-3 and 13 has obviated the previous objections and rejections with respect to these claims.

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

It is suggested that Applicant delete the phrase "AND METHODS OF MAKING AND USING".

Applicant's request, filed 9/30/02, to hold the title change in abeyance is acknowledged.

The requirement for a new title is held in abeyance.

5. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is again acknowledged.

As previously noted, although 60/181,608 provides an adequate written description of the IL-18 epitope defined by instant SEQ ID NO:1 and human monoclonal antibodies to this IL-18 epitope or intact IL-18; the priority document does not appear to support the IL-18 epitopes of SEQ ID NOS:3 or 33 (claims 11-12 and 14-15); nor does it support antibodies comprising at least one CDR or individual antibody species (claims 22-38). Provisional application 60/181,608 also does not appear to provide adequate written support for compounds comprising antibodies to the polypeptides of SEQ ID NO:70 or SEQ ID NO:71 (newly added claim 61).

Therefore, the filing date of claims 11-12, 14-15, 22-38 and 61 appears to be the filing date of the instant application, i.e., 2/9/01.

Applicant is invited to point to adequate support for all limitations of these claims in provisional application 60/181,608.

6. Applicant's amendment, filed 9/30/02, has obviated the previous rejection of claims 1-3, 11-15 and 46 under 35 U.S.C. 112, second paragraph.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 22-38 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein.

Applicant's arguments, filed 9/30/02, have been fully considered but have not been found persuasive for the reasons of record set forth in Paper No. 10.

Applicant argues that because page 12 at lines 4-28 make mention of an isolated CDR as an "antigen-binding portion" of an antibody; this mention suffices to provide adequate written description of the instant claims.

As previously noted, claims 22-38 recite in various forms an antibody or antigen-binding portion thereof comprising "at least one variable region CDR" or "a CDR domain selected from the group consisting of" or variable regions comprising SEQ ID NOS that are individual CDR domains. Thus claims 22-38 recite in some form "an antibody in which fewer than all CDRs are defined".

Applicant has disclosed antibodies in which all three CDRs of the heavy chain variable region and all three CDRs of the light chain variable region are defined. Although a limited number of changes are made to individual CDRs, these changes are always made in the context of a total of six CDRs in any given antibody. Applicant does not appear to describe any antibodies in which fewer than six CDRs are defined and which have the function of binding IL-18 or a peptide comprising an epitope of IL-18.

Thus the minimal structure which provides the function of IL-18 or IL-18 epitope binding appears to include six CDRs (three in the heavy chain variable region and three in the light chain variable region).

Applicant appears to acknowledge that all six CDRs are required for the recited function in the response filed 3/28/02 (see the comments on pages 4-5 regarding election of species).

Thus the ordinary artisan would not recognize Applicant to be in possession of an antibody or antigen-binding fragment thereof that binds human IL-18 or an epitope of human IL-18, unless all six CDRs are defined.

Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Further, claims do not meet the written description requirement simply because they are in ipsis verbis supported by the specification. Even if a claim is supported by the specification, the language of the claim must describe the invention so that one skilled in the art can recognize what is claimed. The appearance of the words of the claim in the specification or as an original claim does not necessarily satisfy that requirement.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

The rejection is maintained for the reasons of record.

9. Claims 22-38 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies and antigen-binding fragments thereof in which the three CDRs in the heavy chain variable region and the three CDRs in the light chain variable region are all defined by a single antibody which binds the relevant antigen (human IL-18 or a peptide epitope thereof) and for mutants of these antibodies in which a limited number of defined changes are made in one or more CDRs; does not reasonably provide enablement for antibodies and antigen-binding fragments thereof that comprise less than three heavy chain CDRs and three light chain CDRs defined by the amino acid sequence of a parental antibody that binds the same antigen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments, filed 9/30/02, have been fully considered but have not been found persuasive for the reasons of record set forth in Paper No. 10.

Applicant again notes that page 12 at lines 4-28 make mention of an isolated CDR as an "antigen-binding portion" of an antibody. Applicant further argues in conjunction with Ward et al. (Nature 1989; 341:544-546) that all six CDRs are not necessarily required for antigen binding because isolated VH domains (comprising only the three CDRs of the heavy chain variable region) are demonstrated by Ward et al. to also bind antigen.

Applicant concludes that because the art provides an example in which fewer than six CDRs can form an antigen-binding compound, the instant specification is enabling.

As previously noted, Claims 22-38 recite in various forms an antibody or antigen-binding portion thereof comprising "at least one variable region CDR" or "a CDR domain selected from the group consisting of" or variable regions comprising SEQ ID NOS that are individual CDR domains. Thus claims 22-38 recite in some form "an antibody in which fewer than all CDRs are defined".

The breadth of the instant claims encompass antibodies or antigen-binding fragments thereof in which fewer than all of the six CDRs found in the heavy plus light chain pair that forms the binding region of a referenced antibody are defined.

As noted supra, Applicant has disclosed antibodies in which all three CDRs of the heavy chain variable region and all three CDRs of the light chain variable region are defined. Although a limited number of changes are made to individual CDRs (e.g., the mutations described in Table 12), these changes are always made in the context of a total of six CDRs in any given antibody derived from a reference antibody that binds IL-18 or an epitope thereof.

The state of the art recognized that, in general, all three CDRs of the heavy chain variable region and all three CDRs of the light chain variable region were important for determining the ability of the antibody to bind antigen. For example, Bendig (Methods: A Companion to Methods in Enzymology 1995; 8:83-93, of record) reviews that the general strategy for "humanizing" antibodies involves the substitution of all six CDRs from a rodent antibody that binds an antigen of interest, and that all six CDRs are involved in antigen binding (see entire document, but especially Figures 1-3). While the instant antibodies are fully human, the same considerations apply to human antibodies defined only based upon CDR sequences.

The Examiner acknowledges the teachings of Ward et al. (ibid). However, the teachings of Ward et al., although presented as an approach which may possibly be generally applicable, provides only limited examples to in which fewer than all six CDRs form an antigen binding structure that binds a particular antigen. The art as a whole does not appear to support the approach of Ward et al. Applicant provides no working examples with respect to the instant antibodies that show that fewer than all six CDRs provides the function of antigen binding. Further, Applicant appears to acknowledge that all six CDRs are required for the recited function in the response filed 3/28/02 (see the comments on pages 4-5 regarding election of species). In addition, it is noted that the teachings of Ward et al. at most address only VH domains, which comprise three CDRs, all derived from the same variable region sequence.

A single teaching of a specific combination and number of CDRs, taken in the context of a body of literature indicating that, in general, all six CDRs are required for antigen binding does not negate the fact that, in general, all six CDRs are required. Thus even in view of the teachings of Ward et al., the skilled artisan must still conclude that it is highly unpredictable that fewer than all six CDRs from an antibody with a desired specificity would bind the same antigen.

In addition, the skilled artisan recognized that single CDRs with the same amino acid sequence could be found in antibodies with diverse specificities. In particular, antibodies which have not yet undergone affinity maturation may still utilize germline heavy and light chain sequences. Between antibodies utilizing the same germline heavy or light chain gene the skilled artisan would expect to find that one or more of the heavy and/or light chain CDRs were the same as that of an antibody with a different specificity, particularly CDRs 1and 2 which are germline encoded completely in the variable region. However, the same CDR may also occur in antibodies having somatic mutations that bind different antigens.

For example, an anti-tumor antibody taught by Garen et al. (US Pat. No. 6,140,470, of record) has the heavy chain set forth in SEQ ID NO:32 of the Garen et al. patent. The heavy chain of SEQ ID NO:32 has the same CDR1 and CDR2 sequences as the heavy chain of the instant anti-IL-18 antibody LT28 (instant SEQ ID NO:28, comprising CDR1 defined by SEQ ID NO:20 and CDR2 defined by SEQ ID NO:21). Thus it would be highly unpredictable that an antibody comprised of fewer than all six CDRs (three CDRs defined in the heavy chain variable region and three CDRs defined in the light chain variable region) of a particular reference antibody would have the same specificity as the reference antibody.

The specification as filed provides no working examples showing that fewer than all six CDRs are required for binding to IL-18 or an epitope thereof. Neither does the specification appear to provide sufficient guidance as to which subsets of CDRs could be used in an antibody comprising less than all six

CDRs from an antibody having IL-18 binding specificity and still maintain IL-18 binding. Without sufficient guidance, it would require undue experimentation of the skilled artisan to make antibodies or antigen-binding fragments thereof which could bind IL-18 and be used in methods of inhibiting IL-18 function that comprised fewer than all six CDRs from a parental antibody that bound IL-18.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Given the recognized unpredictable nature of making antibodies with a desired specificity having fewer than all six CDRs from a reference antibody and the lack of sufficient guidance provided in the specification; the experimentation left to those skilled in the art, is unnecessarily, and improperly, extensive and undue.

The rejection is maintained for the reasons of record.

10. Applicant's amendment, filed 9/30/02 and adding the limitation that the antibody be "human" has obviated the previous rejection of claims 11-12 and 14-15 are rejected under 35 U.S.C. 102(a) as being anticipated by Ho et al. (WO00/56771 #A2, 28 Sept 2000, see entire document).

However, regarding the rejection of record it is noted that the claims 11-12 and 14-15 do not appear to be entitled to an effective filing date of 2/10/00, as asserted by Applicant in the Response filed 9/30/02.

11. Applicant's amendment, filed 9/30/02 and adding the limitation that the antibody be "human" has obviated the previous rejection of claims 16-21 under 35 U.S.C. 102(a) as being anticipated by Yoshihiro et al. (EP 0 974 600 A2, IDS #A1, 26 Jan 2000, see entire document).

12. Applicant's amendment, filed 9/30/02 and adding the limitation that the antibody be "human" has obviated the previous rejection of claims 11-12 and 14-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Yoshihiro et al. (EP 0 974 600 A2, IDS #A1, 26 Jan 2000, see entire document).

However, regarding the rejection of record it is noted that the claims 11-12 and 14-15 do not appear to be entitled to an effective filing date of 2/10/00, as asserted by Applicant in the Response filed 9/30/02.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 4-12, 14-24, 44-46 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kucherlapati et al. (US Pat No. 6,075,181, of record) and Dinarello et al. (J. Leukoc. Biol. 1998; 63:658-664, IDS #A4).

Applicant's arguments, filed 9/30/02, have been fully considered but have not been found convincing.

Applicant's arguments are addressed in the context of the reiteration of the rejection of record, as applied to the amended claims.

The instant claims are drawn to human antibodies to human IL-18 having various functional properties in terms of their binding to IL-18.

As previously noted, Kucherlapati et al. teach a method of producing fully human monoclonal antibodies to any protein of interest, but especially cytokines, by using the protein to immunize mice which express human antibody genes (see entire document, but especially columns 8-9. Kucherlapati et al. teach that fully human monoclonal antibodies are highly advantageous compared to rodent antibodies or even humanized antibodies for therapeutic applications, because administration of human antibodies to humans avoids the undesired immune responses elicited by administering non-human antibodies to humans (see column 8, especially lines 21-41).

Kucherlapati et al. also teach that the human antibody genes can be cloned and used to produce recombinant, fully human, monoclonal antibodies, e.g., for phage display libraries (e.g., columns 6-7). Kucherlapati et al. teach that such recombinant human antibodies offer the advantage that phage libraries can be screened for selection of antibodies with the highest affinity to the antigen of interest, or can be manipulated to increase the affinity of the antibody for the antigen (e.g., column 7, especially the comment at lines 58-65).

Kucherlapati et al. do not teach human antibodies to IL-18.

Applicant notes that Kucherlapati et al. issued and published on 13 June 2000, which is after the 2 Feb. 2000 filing date of Applicant's provisional application.

The Examiner acknowledges the issue date of Kucherlapati et al. is 13 June 2000. However, Kucherlapati et al. was filed on 07 June 1995. Thus Kucherlapati et al. is available as a prior art reference *as of its filing date* under 35 USC 102(e), irrespective of the changes made to 35 U.S.C. 102(e) by the American

Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002.

The application of Kucherlapati et al. as a prior art reference in the context of a rejection under 35 USC 103(a) is therefore appropriate.

Dinarello et al. teach that human IL-18 had been cloned and produced recombinantly (see e.g. page 659 "Molecular cloning of IGIF"). Dinarello et al. review that IL-18 initiates the Th1 inflammatory cytokine cascade, leading to the production of later cytokine mediators such as TNF-α, IL-1 and IL-8, and that antibodies to IL-18 can inhibit the in vivo production of other cytokines such as TNF-α (e.g. page 660, right column). Dinarello et al. note that given what is known about the role of cytokines such as TNF-α, IL-1 and IL-8 that are induced by IL-18 in human disease such as rheumatoid arthritis and Crohn's Disease; that preventing the activity of IL-18 which induces these other cytokines is a sensible clinical strategy (e.g., page 662 "What is the clinical importance of the pro-inflammatory cytokine IL-18?). Dinarello et al. also note in this discussion of the clinical importance of inhibiting IL-18 activity that neutralizing anti-IL-18 antibodies are a therapeutic option for inhibiting IL-18 activity.

Therefore, it would have been obvious to the ordinary artisan at the time the invention was made to produce human antibodies to human IL-18 that were capable of neutralizing the activity of IL-18. Recombinant IL-18 was known in the art at the time the invention was made, as taught by Dinarello et al. Kucherlapati et al. provide a method of producing fully human antibodies to human cytokines. Thus the ordinary artisan at the time the invention was made would have had a reasonable expectation that, given the availability of recombinant human IL-18, fully human antibodies to human IL-18 could be produced using the method of Kucherlapati et al.

The ordinary artisan at the time the invention was made would have been motivated to produce fully human monoclonal antibodies that could bind to and neutralize human IL-18 in order to provide a therapeutic reagent that could be administered to humans without eliciting the undesirable immune responses associated with the administration of rodent or even humanized rodent antibodies, as taught by Kucherlapati et al. The desirability of neutralizing antibodies to human IL-18 is clearly taught by Dinarello et al.

Further, the ordinary artisan at the time the invention was made would have been motivated to provide recombinant forms of the fully human antibodies so that the binding affinity and ability of the antibody to neutralize human IL-18 could be improved by successive rounds of manipulation and screening of phage display libraries of the human anit-IL-18 monoclonal antibodies. Although monoclonal antibodies typically have k_{off} rate constants as measured by surface plasmon resonance and inhibition activity with an IC_{50} in the ranges recited, using the affinity maturation approach as taught by Kucherlapati et al would have ensured that the ordinary artisan would have obtained human antibodies that bound human IL-18 and had k_{off} rate constants of $1x10^{-6}s^{-1}$ and IC_{50} values of $1x10^{-11}M$. Further, the affinity modifications taught by Kucherlapati et al. would have resulted in at least one amino acid substitution or insertion that improves the IL-18 binding as compared to the original antibody. Any human anti-human IL-18 antibody would of necessity possess at least one variable region CDR domain capable of binding an epitope of human IL-18, and would bind an epitope of human IL-18 comprising SEQ ID NOS:3, SEQ ID NO:33, SEQ ID NO:70 or SEQ ID NO:71 since SEQ ID NOS:3, 33, 70 and 71 are each subsequences of human IL-18.

Finally, given that the ordinary artisan would have been motivated to provide human monoclonal antibodies to human IL-18 because of their therapeutic potential in inflammatory diseases, as taught by Dinarello et al.; the ordinary artisan would have clearly been motivated to formulate the human anti-human IL-18 antibody in a pharmaceutical composition. The addition of at least one additional

therapeutic agent already shown to have some efficacy against these inflammatory diseases, e.g., the addition of methotrexate or anti-TNFα for the treatment of rheumatoid arthritis, would have also been an obvious combination at the time the invention was made to provide a more efficacious therapeutic composition.

While Applicant's Remarks, filed 9/30/02 regarding the failure of Dinarello et al. to teach human antibodies are acknowledged, the combination of Dinarello et al. and Kucherlapati et al. do clearly render human antibodies to human IL-18 obvious. Therefore, for the reasons set forth supra, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The rejection of record, as applied to the amended claims, is maintained.

15. No claim is allowed.

16. It is again noted that claims drawn to the following anti-IL-18 antibodies would appear to be free of the art:
1) an antibody comprising the heavy chain variable region defined by SEQ ID NO:18 and the light chain variable region defined by SEQ ID NO:19;
2) an antibody comprising the heavy chain variable region defined by SEQ ID NO:28 and the light chain variable region defined by SEQ ID NO:29;
3) an antibody comprising a heavy chain variable region in which the CDRs are defined by SEQ ID NOS:9-11 and a light chain variable region in which the CDRs are defined by SEQ ID NOS:12-14; and
4) an antibody comprising a heavy chain variable region in which the CDRs are defined by SEQ ID NOS:20-22 and a light chain variable region in which the CDRs are defined by SEQ ID NOS:23-25.

17. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. This application contains claims 39-43 and 47-60 drawn to an invention nonelected with traverse in Paper No. 9. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica H. Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday, 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
December 11, 2002

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12/16/02